## **Uses and Administration**

Flufenamic acid, an anthranilic acid derivative related to mefenamic acid (p.80), is an NSAID (p.99). Flufenamic acid is mainly used topically in a concentration of 3 or 3.5% for the relief of pain and inflammation associated with musculoskeletal. joint, and soft-tissue disorders. Flufenamic acid and its aluminium salt have also been given orally.

### **Preparations**

Proprietary Preparations (details are given in Part 3) Ger.: Dignodolin†; Jpn: Opyrin

Multi-ingredient: Austria: Mobilisin; Mobilisin plus; Rheugesal; Belg.: Mobilisin; Braz.: Mobilisin Composto; Ger.: Algesalona†; Hung.: Mobilisin; Spain: Mobilisin; Port.: Latesil; Mobilisin; Spain: Movilisin; Switz.: Algesalona†; Assan; Assan thermo; Mobilisin.

## Flunixin Meglumine (BANM, USAN, rINNM)

Fluniksiinimeglumiini; Flunixin megluminová sůl; Flunixine méglumine; Flunixini megluminum; Flunixinmeglumin; Flunixino meglumina; Flunixinum Megluminicum; Meglumini Flunixinum; Sch-14714 (flunixin). 2-{[2-Methyl-3-(trifluoromethyl)phenyl]amino}-3-pyridinecarboxylic acid compounded with 1-deoxy-1-(methylamino)-D-glucitol (1:1);  $2-(\alpha^3,\alpha^3,\alpha^3-\text{Trifluoro}-2,3,-\text{xylidino})$ nicotinic acid compounded with I-deoxy-I-(methylamino)-D-glucitol

Меглумина Флуниксин

 $C_{14}H_{11}F_3N_2O_2, C_7H_{17}NO_5 = 491.5.$ CAS — 38677-85-9 (flunixin); 42461-84-7 (flunixin meg-

(flunixin)

**Pharmacopoeias.** In Eur. (see p.vii) and US for veterinary use

Ph. Eur. 6.2 (Flunixin Meglumine for Veterinary Use; Flunixin Meglumine BP(Vet) 2008). A white to almost white crystalline powder. Freely soluble in water and in methyl alcohol: practically insoluble in acetone. A 5% solution in water has a pH of 7.0 to

USP 31 (Flunixin Meglumine). A white to off-white crystalline powder. Soluble in water, in alcohol, and in methyl alcohol; practically insoluble in ethyl acetate. pH of a 5% solution in water is between 7.0 and 9.0. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Flunixin meglumine is an NSAID (p.96) used in veterinary medicine for the relief of pain and inflammation in acute and chronic disorders and as adjunctive therapy in the treatment of endotoxic or septic shock and mastitis.

## Flupirtine Maleate (BANM, USAN, rINNM)

D-9998; Flupirtine, Maléate de; Flupirtini Maleas; Maleato de flupirtina; W-2964M. Ethyl 2-amino-6-(4-fluorobenzylamino)-3-pyridylcarbamate maleate.

Флупиртина Малеат

 $C_{15}H_{17}FN_4O_2$ ,  $C_4H_4O_4 = 420.4$ .

CAS — 56995-20-1 (flupirtine); 75507-68-5 (flupirtine maleate).

ATC - NO2BG07

ATC Vet — QN02BG07.

(flupirtine)

## **Profile**

Flupirtine maleate is an analgesic that has been given for the relief of pain (see Choice of Analgesic, p.2) in usual doses of 100 mg three or four times daily by mouth, or 150 mg three or four times daily as a rectal suppository; daily doses of up to  $600~\rm mg$  by mouth or  $900~\rm mg$  rectally have been used where necessary. Flupirtine has also been given by intramuscular injection as the gluconate in the management of acute pain.

There has been some interest in the potential of flupirtine to treat prion diseases such as Creutzfeldt-Jakob disease (see below).

1. Friedel HA, Fitton A. Flupirtine: a review of its pharmacological properties, and therapeutic efficacy in pain states. Drugs 1993; **45:** 548–69.

Creutzfeldt-Jakob disease. A double-blind placebo-controlled study<sup>1</sup> in 28 patients with Creutzfeldt-Jakob disease (CJD) found flupirtine to have beneficial effects on cognitive function. However, further studies are needed to establish any place in

 Otto M, et al. Efficacy of flupirtine on cognitive function in pa-tients with CJD: a double-blind study. Neurology 2004; 62: 714-18.

## **Preparations**

Proprietary Preparations (details are given in Part 3) Braz.: Katadolon; Ger.: Katadolon; Trancopal Dolo; Port.: Metanor; No vocebrin; **Rus.:** Katadolon (Катадолон).

# Flurbiprofen (BAN, USAN, rINN)

BTS-18322; Flurbiprofeeni; Flurbiprofén; Flurbiprofenas; Flurbiprofène; Flurbiprofeno; Flurbiprofenum; U-27182. 2-(2-Fluorobiphenyl-4-yl)propionic acid.

Флурбипрофен

 $C_{15}H_{13}FO_2 = 244.3.$ 

CAS - 5104-49-4.

ATC - MOIAE09; MO2AAI9; SOIBCO4.

ATC Vet — QM01AE09; QM02AA19; QS01BC04.

Pharmacopoeias. In Eur. (see p.vii), Jpn, and US.

Ph. Eur. 6.2 (Flurbiprofen). A white or almost white crystalline powder. Practically insoluble in water; freely soluble in alcohol and in dichloromethane; dissolves in aqueous solutions of alkali hydroxides and carbonates.

**USP 31** (Flurbiprofen). A white crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, in ether, and in methyl alcohol; soluble in acetonitrile. Store in airtight containers.

# Flurbiprofen Sodium (BANM, rINNM)

Flurbiprofène Sodique; Flurbiprofeno sódico; Natrii Flurbiprofenum. Sodium (±)-2-(2-fluoro-4-biphenylyl)propionate dihydrate. Натрий Флурбипрофен

 $C_{15}H_{12}FNaO_2, 2H_2O = 302.3.$ CAS — 56767-76-1.

Pharmacopoeias. In Br: and US.

BP 2008 (Flurbiprofen Sodium). A white to creamy-white, crystalline powder. Sparingly soluble in water; soluble in alcohol; practically insoluble in dichloromethane.

## **Adverse Effects and Treatment**

As for NSAIDs in general, p.96.

Minor symptoms of ocular irritation including transient burning and stinging have been reported on instillation of flurbiprofen sodium eye drops; there may be increased bleeding from ocular surgery and wound healing may be delayed. Local irritation has also followed rectal use, and local effects including a sensation of warming or burning in the mouth may be seen after using flurbiprofen lozenges.

Incidence of adverse effects. Reports from the manufacturers on the range and incidence of the adverse effects of flurbiprofen.1,2

- Sheldrake FE, et al. A long-term assessment of flurbiprofen. Curr Med Res Opin 1977; 5: 106–16.
- Brooks CD, et al. Clinical safety of flurbiprofen. J Clin Pharma-col 1990; 30: 342–51.

Effects on the CNS. A severe symmetrical parkinsonian syndrome developed in a 52-year-old man who had taken flurbiprofen for 7 days.1

1. Enevoldson TP, et al. Acute parkinsonism associated with flurbiprofen. BMJ 1990; **300:** 540-1.

Effects on the kidneys. Renal papillary necrosis has been described in a patient who had used flurbiprofen for many years. Acute flank pain and reversible renal dysfunction has been reported in 2 patients treated with flurbiprofen.<sup>2,3</sup> Membranous nephropathy also developed in a patient who took flurbiprofen daily for 12 to 18 months.4

Nafría EC, et al. Renal papillary necrosis induced by flurbipro-fen. DICP Ann Pharmacother 1991; 25: 870-1.

Kaufhold J, et al. Flurbiprofen-associated tubulointerstitial ne-phritis. Am J Nephrol 1991; 11: 144–6.

- McIntire SC, et al. Acute flank pain and reversible renal dysfunction associated with nonsteroidal anti-inflammatory drug use. Pediatrics 1993; 92: 459–60.
- MacKay K. Membranous nephropathy associated with the use of flurbiprofen. Clin Nephrol 1997; 47: 279–80.

Effects on the liver. A case of cholestatic jaundice probably due to flurbiprofen has been reported.1

1. Kotowski KE, Grayson MF. Side effects of non-steroidal antiinflammatory drugs. BMJ 1982; 285: 377.

Effects on the skin. Cutaneous vasculitis apparently due to flurbiprofen occurred in a 59-year-old woman with long-standing rheumatoid arthritis.1 Contact dermatitis has also been seen in a 22-year-old woman who applied a poultice containing flurbiprofen to her wrist.2

- 1. Wei N. Flurbiprofen and cutaneous vasculitis. *Ann Intern Med* 1990; **112:** 550–1.
- 2. Kawada A, et al. Contact dermatitis due to flurbiprofen. Contact Dermatitis 2000; 42: 167–8

Hypersensitivity. A diffuse, pruritic, maculopapular rash developed in a patient 48 hours after taking a second dose of flurbiprofen.1 Two days later, the rash had become urticarial, and angioedema and hypotension were also noted. Patch testing with flurbiprofen powder was positive.

See also Effects on the Skin, above.

Romano A, Pietrantonio F. Delayed hypersensitivity to flurbi-profen. J Intern Med 1997; 241: 81–3.

## **Precautions**

As for NSAIDs in general, p.98.

Breast feeding. Flurbiprofen is distributed into breast milk; however, the BNF and licensed product information consider the amount to be too small to be harmful to a breast-fed infant.

Herpes simplex keratitis. Whether flurbiprofen can exacerbate infection when used to treat ocular herpes simplex is unclear from *animal* studies, <sup>1,2</sup> but licensed product information for flurbiprofen sodium eye drops recommends that they should not be used in patients with active epithelial herpes simplex keratitis. Patients with a history of herpes simplex keratitis should also be monitored closely when undergoing treatment with these eye

- Trousdale MD, et al. Effect of flurbiprofen on herpes simpler keratitis in rabbits. Invest Ophthalmol Vis Sci 1980; 19: 267–70.
- Hendricks RL, et al. The effect of flurbiprofen on herpes simplex virus type 1 stromal keratitis in mice. Invest Ophthalmol Vis Sci 1990; 31: 1503–11.

## Interactions

For interactions associated with NSAIDs, see p.99.

Parasympathomimetics. Licensed product information for acetylcholine chloride ophthalmic preparations and for flurbiprofen sodium eye drops states that there have been reports that acetylcholine and carbachol have been ineffective when used in patients treated with topical (ophthalmic) NSAIDs.

## **Pharmacokinetics**

Flurbiprofen is readily absorbed from the gastrointestinal tract after oral doses with peak plasma concentrations occurring about 1 to 2 hours after ingestion. Absorption after rectal doses may be more rapid. It is about 99% bound to plasma proteins and has a plasma half-life of about 3 to 6 hours. It is metabolised mainly by hydroxylation (via the cytochrome P450 isoenzyme CYP2C9) and conjugation in the liver and excreted in urine. Flurbiprofen is distributed into breast milk.

Flurbiprofen is a chiral compound given as the racemate and the above pharmacokinetic characteristics refer to the racemic mixture. Allowance may have to be made for the different activities of the enantiomers.

- 1. Aarons L, et al. Plasma and synovial fluid kinetics of flurbiprofen in rheumatoid arthritis. Br J Clin Pharmacol 1986; 21: 155-63
- 2. Smith IJ, et al. Flurbiprofen in post-partum women: plasma and breast milk disposition. *J Clin Pharmacol* 1989; **29:** 174–84.

  3. Kean WF, *et al.* The pharmacokinetics of flurbiprofen in younger
- and elderly patients with rheumatoid arthritis. *J Clin Pharmacol* 1992; **32:** 41–8.

  4. Davies NM. Clinical pharmacokinetics of flurbiprofen and its
- enantiomers. Clin Pharmacokinet 1995; 28: 100-14.

## Uses and Administration

Flurbiprofen, a propionic acid derivative, is an NSAID (p.99). It is used in musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis, in soft-tissue disorders such as sprains and strains, for postoperative pain, and in mild to moderate pain including dysmenorrhoea and migraine. Flurbiprofen is also used as lozenges in the

symptomatic relief of sore throat. Flurbiprofen sodium is used in eye drops to inhibit intra-operative miosis and to control postoperative inflammation of the anterior segment of the eye.

For pain and inflammation, flurbiprofen is given in usual oral doses of 150 to 200 mg daily in divided doses, increased to 300 mg daily in acute or severe conditions if necessary. A modified-release preparation for once-daily use is also available. Patients with dysmenorrhoea may be given an initial dose of 100 mg followed by 50 to 100 mg every four to six hours to a maximum total daily dose of 300 mg. Doses given rectally as suppositories are similar to those given by orally.

For the relief of sore throat, a lozenge containing 8.75 mg of flurbiprofen may be sucked or allowed to dissolve slowly in the mouth every 3 to 6 hours to a maximum daily dose of 5 lozenges. It is recommended that treatment should be limited to a maximum of 3

To inhibit intra-operative miosis during ocular surgery one drop of flurbiprofen sodium 0.03% is instilled into the eye every 30 minutes beginning 2 hours before surgery and ending not less than 30 minutes before surgery. To control postoperative inflammation the same dosage regimen is used before ocular surgery followed 24 hours after surgery by the instillation of one drop 4 times daily for 1 to 3 weeks. Flurbiprofen sodium eye drops have also been used in the topical treatment of cystoid macular oedema.

Flurbiprofen axetil has been given in some countries by intravenous injection for severe pain.

The *R*-enantiomer, tarenflurbil, is under investigation in the management of Alzheimer's disease.

## **Preparations**

**BP 2008:** Flurbiprofen Eye Drops; Flurbiprofen Suppositories; Flurbiprofen USP 31: Flurbiprofen Sodium Ophthalmic Solution; Flurbiprofen Tablets.

# Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)

Arg.: Clinadoi: Flurbic; Flurbict; Luarprofeno; Tolerane; Austral.: Ocufen; Strepfen; Austria: Froben; Ocuflur; Belg.: Froben; Ocuflur; Braz.: Ocufen; Targus; Canad.: Ansaid; Froben; Novo-Flurprofen; Ocuflur; Braz.: Ocufen; Targus; Canad.: Ansaid; Flugalin; Ocuflur; Strepfen; Care. Obendan Direkt; Dobrofen; Ocuflur; Gr.: Bedicet; Bonatol-R; Fladolef-B; Flurofen; Cluroptic; Infallur; Ocuflur; Gr.: Bedicet; Bonatol-R; Fladolef-B; Flurofen; Cluroptic; Infallur; Cucflur; Hong Kong; Ocufen; Hung.: Flugalin; Ocuflur; Strepfen; India: Arflurt; Cadiflur; Froben; Ocuflur; Inf.: Froben; Ocufen; Strepfen; Renzo; Ocufen; Strepfen; Pol.: Flurofen; Ocufen; Strepfen; Pol.: Flurofen; Tarsact Lat; Jan.: Strepfen; Froben; Ocufen; Strepfen; Pol.: Flurofen; Transact Lat; Rus.: Strepfen (Crpenфen); S.Afr.: Froben; Ocufen; Transact Lat; Rus.: Strepfen (Crpenфen); S.Afr.: Froben; Ocufen; Transact Lat; Rus.: Strepfen; Ocuflur; Reupac; Trush; Moo Artorl; Ocuflur; Mutt.: Froben; Ocufen; Transact Lat; Rus.: Strepfen; Ocuflur; Reupac; Froben; Ocufen; Transact Lat; Rus.: Strepfen; Ocuflur; Reupac; Froben; Ocufen; Strepfen; Ocuflur; Reupac; Froben; Ocufen; Strepfen; Ocufen; Strepfen; Ocuflur; Reupac; Froben; Ocufen; Strepfen; Ocufen; Strepfen; Ocufen; Strepfen; USA: Ansaid; Ocufen; Venez.: Flurben; Ocufen;

## Fosfosal (MNN)

Fosfosalum; UR-1521. 2-Phosphono-oxybenzoic acid.

Φοσφοσαλ

 $C_7H_7O_6P = 218.1.$ CAS - 6064-83-1.

Fosfosal is a salicylic acid derivative (see Aspirin, p.20). It has been given in usual oral doses of up to 3.6 g daily for the treatment of pain.

## **Preparations**

Proprietary Preparations (details are given in Part 3) Spain: Aydolid; Disdolen; Protalgia.

Multi-ingredient: Spain: Aydolid Codeina; Disdolen Codeina.

### **Furprofen**

Furprofeno. 4-(2-Furanylcarbonyl)- $\alpha$ -methylbenzeneacetic acid. Фурпрофен

 $C_{14}H_{12}O_4 = 244.2.$ CAS — 66318-17-0.

Furprofen, a propionic acid derivative, is an NSAID (p.96) that has been given by mouth for the relief of pain.

### **Preparations**

Proprietary Preparations (details are given in Part 3) Ital.: Dolext

### Glafenine (HNN)

Glafenina; Glafénine; Glafeninum; Glaphenine. 2,3-Dihydroxypropyl N-(7-chloro-4-quinolyl)anthranilate.

Глафенин

 $C_{19}H_{17}CIN_2O_4 = 372.8.$ 

CAS — 3820-67-5.

ATC - N02BG03.

ATC Vet - QN02BG03.

Glafenine, an anthranilic acid derivative, is an NSAID (p.96) that was used for the relief of all types of pain. However, its high incidence of anaphylactic reactions has led to its withdrawal from the market in most countries. Glafenine hydrochloride was also

Adverse effects and precautions. Glafenine is a common cause of anaphylaxis. There may be hepatotoxicity (sometimes fatal), nephrotoxicity, and gastrointestinal disturbances. It should be stopped at the first sign of any allergic reaction. Crystallisation of glafenine in the urinary tract has also occurred. Cross-reactivity with floctafenine has been reported.

## Glucametacin (HNN)

Glucametacina; Glucamétacine; Glucametacinum. 2-{2-[1-(4-Chlorobenzoyl)-5-methoxy-2-methylindol-3-yl]acetamido}-2deoxy-D-glucose

Глюкаметацин

 $C_{25}H_{27}CIN_2O_8 = 518.9.$ 

\_ 52443-21*-*7.

## **Profile**

Glucametacin, a derivative of indometacin (p.66), is an NSAID (p.96) that has been given orally in musculoskeletal, joint, periarticular, and soft-tissue disorders.

## **Preparations**

Proprietary Preparations (details are given in Part 3)

Braz.: Teoremin: Mex.: Teoren

Multi-ingredient: Chile: Fibrorelax.

## Glycol Salicylate

Ethylene Glycol Monosalicylate; Glycoli Salicylas; Glykolisalisylaatti; Glykolsalicylat; Hidroksietilo salicilatas; Hidroxietil-szalicilát; Hydroksietyylisalisylaatti; Hydroxietylsalicylat; Hydroxyaethyli Salicylas; Hydroxyéthyle, salicylate d'; Hydroxyethylis salicylas; Hydroxyethyl-salicylát; Salicilato de glicol. 2-Hydroxyethyl salicylate.

Гликоль Салицилат

 $C_9H_{10}O_4 = 182.2.$ CAS - 87-28-5.

Pharmacopoeias. In *Eur.* (see p.vii). Ph. Eur. 6.2 (Hydroxyethyl Salicylate). An oily, colourless or almost colourless liquid or colourless crystals. M.p. about 21°. Sparingly soluble in water; freely soluble in alcohol; very soluble in acetone and in dichloromethane. Protect from light.

### **Profile**

Glycol salicylate is a salicylic acid derivative used similarly to methyl salicylate (p.85) in topical rubefacient preparations in usual concentrations of 5 to 15% for the relief of muscular and rheumatic pain. Dipropylene glycol salicylate has been used in

## **Preparations**

### Proprietary Preparations (details are given in Part 3)

Cz.: Lumbinon†; Ger.: Auroanalin N†; Dolo-Arthrosenex N; Dolo-Arthrosenex NH; Dolo-Rubriment H†; Etrat Sportgel HES; Kytta†; Lumbinon†; Mobilat Akut HES; Phardol mono; Phlogont Rheuma†; Phlogont†; Rheubalmin N†; Salhumin Gel; Traumasenex; zuk Schmerzgel, zuk Schmerzsalbet.

Phlogont†; Rheubalmin N†; Salhumin Gel; Traumasenex; zuk Schmerzgel, zuk Schmerzalbe†.

Multi-ingredient: Arg.: Infrarub†; Venostasin; Austral.: Deep Heat; Goanna Analgesic Ice†; Austria: Ambenat: Etrat; Igitur-Rheumafluid; Menthoneurin; Mobilisin; Movillex; Rheumex; Rutzion-Rheumagle; Rubriment; Sportino Akut; Venostasin compositum; Belg.: Algipan; Emenki; Mobilisin; Percutalgine; Rado-Sali; Rado-Spray†; Stilene: Braz.: Etrat†; Mobilisin Composto, Venostasin†; Candd.: Midalgan†; Cz.: Amiolio; Dolo-Rubriment†; Rheuma-Salbe†; Rubriment-N†; Fin.: Movillex†; Fr.: Algipan; Cortisal; Le Thermogene†; Lumbalgine: Percutalgine; Ger.: ABC Warme-Salbe†; Ambene N; Arthrodestal N†; Auroanalin Thermo; Caye Rheuma-Balsam; Dolo Mobilat†; Doloneuror†; Dolo/Visano Salbe†; Essaven Sport†; Etrat Sportgel†; Heparin Plus†; Hot Thermo; Infrotto Ultra†; Lumbinon Thermo†; Rheuma-Balsam†; Phlogont-Thermal; Rheubalmin Thermo†; Phardol Warme-Balsam†; Phlogont-Thermal; Rheubalmin Thermo†; Pharma-Bad; Rheuma-Salbe†; Rubriment-N†; Sportino Akut; Tetesept Badekonzentrat Rheuma Bad†; Thermo-Menthoneurin†; Thermo-Rheumon N†; Thermosenex; Togal Mobil-Gel†; Trauma-Puren†; Venoplant AHS†; Vertebralon N†; Warme-Gel†; zuk thermo†; Gr.: Bayolin; Hong Kong; New Patecs A; Prelloran†; Salomethy; Hung: Bayolin†; Mobilisin; Nicofiex, India: Algipan; Inl.: Algipan; Israel: Deep Heat Spray; Ital: Balsamo Sifcanina: Disalgil†, Mobilisin; Singapore: Deep Heat Spray; India; Salonpas; Sloan; Maloysia: Salonpas; Neth.: Cremor capsic comp; Cremor Capsic compositus; Kruidvat Spierbalsem; Pol.: Deep Heat Spray; Infrarub; Singapore: Deep Heat Spray; India; Sportusal; Sportusal

## Gold Keratinate

Aurothiopolypeptide; Queratinato de oro.

CAS - 9078-78-8.

## **Profile**

Gold keratinate is a gold compound with a gold content of about 13%; It has similar actions and uses to those of sodium aurothiomalate (p.122). It has been given by intramuscular injection as the calcium salt for the treatment of rheumatoid arthritis.

## **Preparations**

Proprietary Preparations (details are given in Part 3) Arg.: Aurochobet

# Golimumab (USAN, rINN)

CNTO-148; Golimumabum. Immunoglobulin G1, anti-(human tumor necrosis factor α) (human monoclonal CNTO 148 γIchain), disulfide with human monoclonal CNTO 148 k-chain, dimer

Голимумаб

CAS - 476181-74-5.

## **Profile**

Golimumab is a human monoclonal antibody to tumour necrosis factor α, a pro-inflammatory mediator (see Infliximab, p.71), that